The role of MRI in pharmacovigilance of natalizumab-treated MS patients: a “known unknown”?

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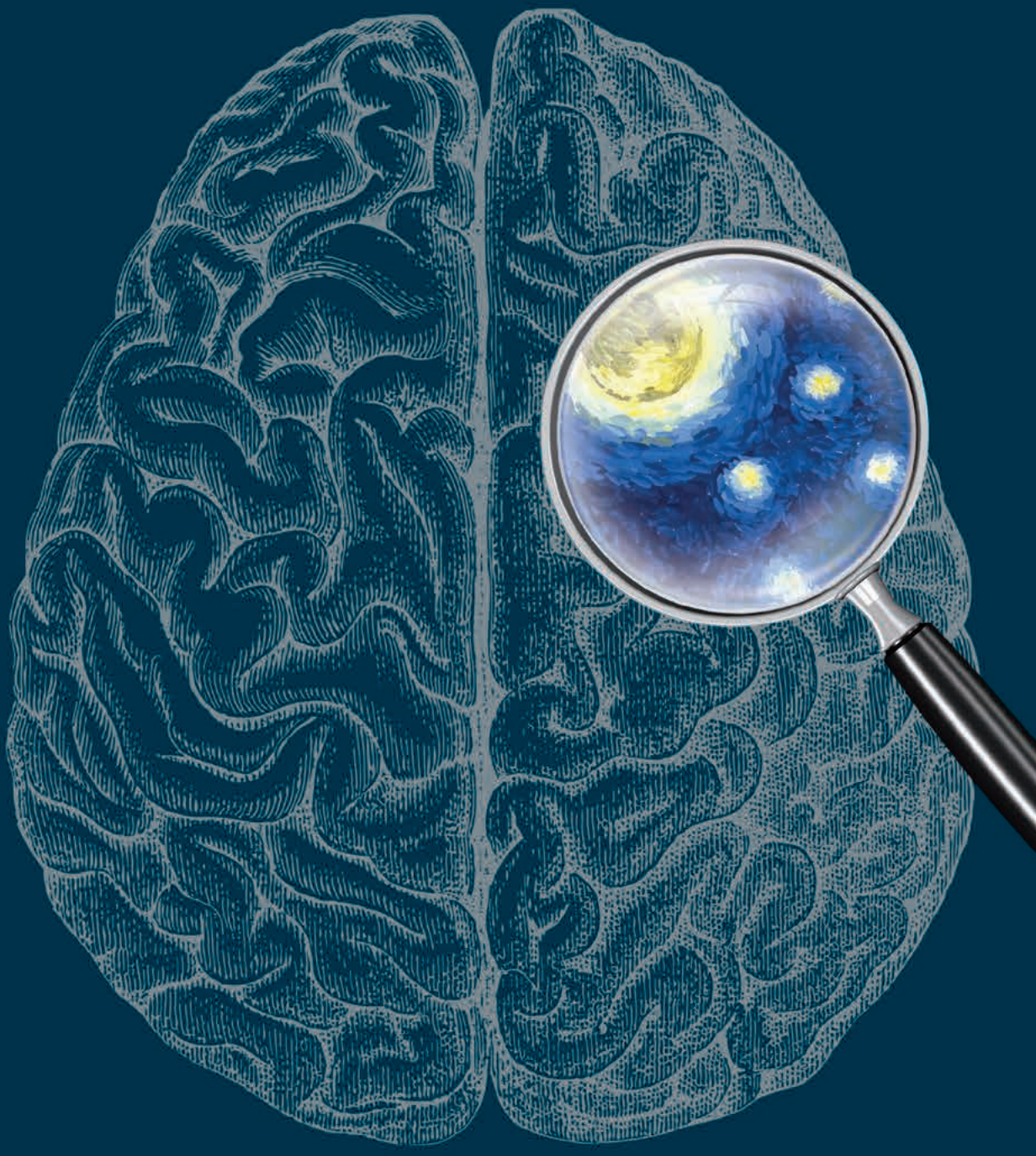

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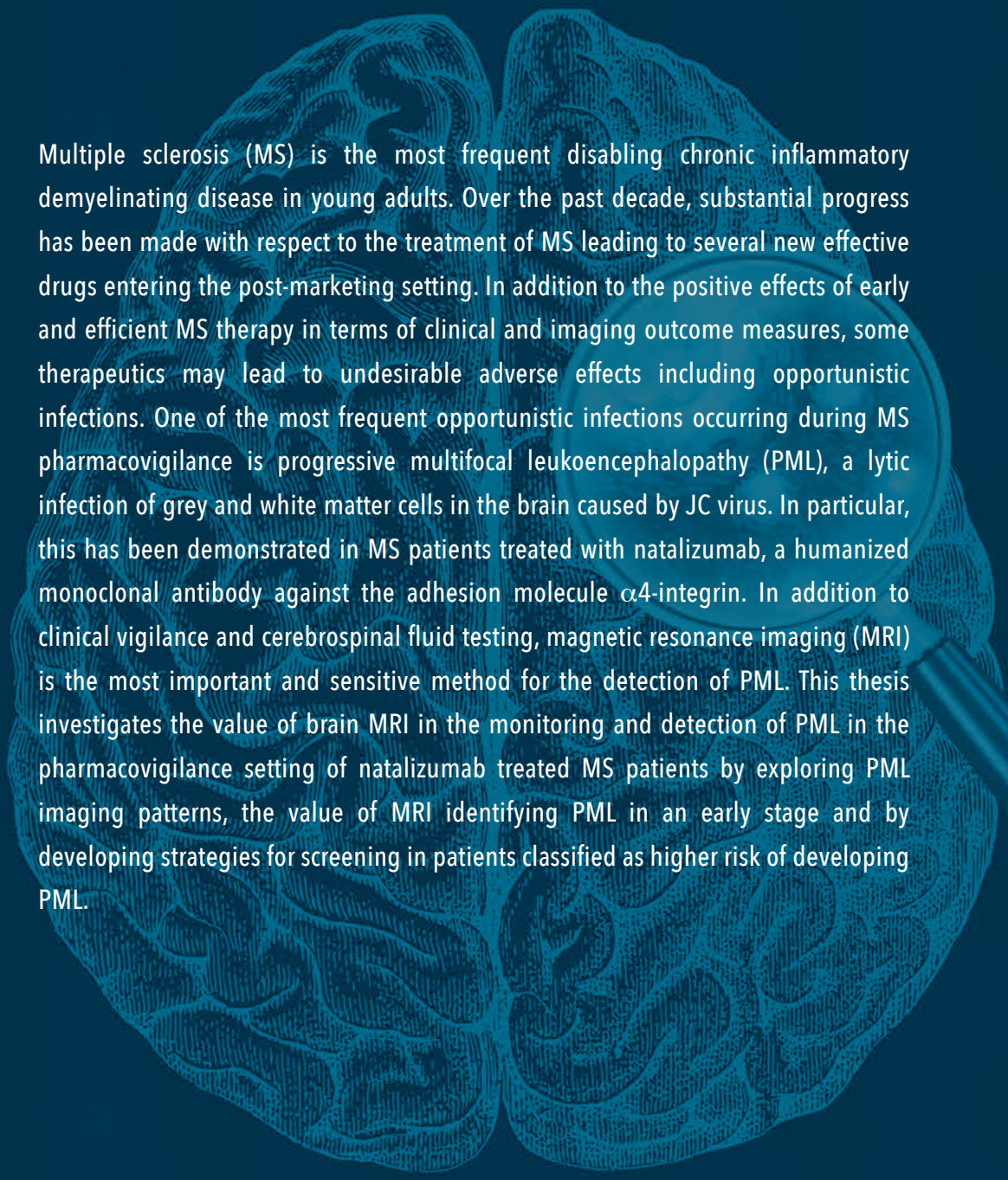

Multiple sclerosis (MS) is the most frequent disabling chronic inflammatory demyelinating disease in young adults. Over the past decade, substantial progress has been made with respect to the treatment of MS leading to several new effective drugs entering the post-marketing setting. In addition to the positive effects of early and efficient MS therapy in terms of clinical and imaging outcome measures, some therapeutics may lead to undesirable adverse effects including opportunistic infections. One of the most frequent opportunistic infections occurring during MS pharmacovigilance is progressive multifocal leukoencephalopathy (PML), a lytic infection of grey and white matter cells in the brain caused by JC virus. In particular, this has been demonstrated in MS patients treated with natalizumab, a humanized monoclonal antibody against the adhesion molecule α4-integrin. In addition to clinical vigilance and cerebrospinal fluid testing, magnetic resonance imaging (MRI) is the most important and sensitive method for the detection of PML. This thesis investigates the value of brain MRI in the monitoring and detection of PML in the pharmacovigilance setting of natalizumab treated MS patients by exploring PML imaging patterns, the value of MRI identifying PML in an early stage and by developing strategies for screening in patients classified as higher risk of developing PML.